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NOVARTIS

Division of Dockets Management
U.S. Food & Drug Administration
HFA-305
5630 Fishers Lane Room 1061
Rockville, MD 20857

Docket 2004N-0535
Novartis comments on proposed changes to MedWatch Form 3500A

February 8, 2005

Dear Sir/Madam:

Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG (NYSE: NVS), a world leader in pharmaceuticals and consumer health. Headquartered in Basel, Switzerland, Novartis Group companies employ about 81,400 people and operate in over 140 countries around the world.

Novartis Pharmaceuticals Corporation researches, develops, manufacturers and markets leading innovative prescription drugs used to treat a number of diseases and conditions, including central nervous system disorders, organ transplantation, cardiovascular diseases, dermatological diseases, respiratory disorders, cancer and arthritis.

As one of the world's largest pharmaceutical manufacturers, Novartis has committed extensive resources to the handling of safety information for its investigational and marketed products. The proposed MedWatch Form 3500A revision will significantly impact our global safety handling operations and we appreciate the opportunity to offer comments on this guideline.

General comments

1. Like many larger pharmaceutical companies, Novartis reports 15-day post-marketing events electronically, and plans to do the same for non-15-day reports beginning in 2005. For spontaneous reports and post-marketing studies, the proposed new MedWatch form would therefore only be used during rare network or server outages to prevent late case submissions. Novartis has also chosen the option of submitting 7/15 day IND alerts on MedWatch forms (the CFR also allows submission in other formats). We currently submit approximately 600 such reports per year. We believe the human and financial resources needed to overhaul what is essentially a low-volume/ emergency reporting form is not an efficient use of resources.

2. The new form requires significant database and source code changes, many of which will need to be completed by vendors who develop pharmacovigilance software packages for the industry. Some examples :

- Creation of new US-only data fields.

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- Extensive r[redacted]apping of each new or revised data field t[redacted]e 3500A.
- Changes to character length and population of hard-coded fields due to re-formatting/ spacing changes to existing fields.
- Complete re-validation of the safety database.

3. Providing relevant and useful comments on the proposed MedWatch revision is limited by the absence of instructions on how the form should be completed and the lack of definitions for new data fields.

4. Several of proposed new data fields are inconsistent with ICH Data Elements for the Transmission of Individual Case Safety Reports. This diverges from the ongoing Tripartite effort to limit local customization of E2B files. At minimum the new fields should be reviewed and commented on as part of the formal ICH process.

5. It should be clarified if drug manufacturers will still be allowed to customize the form by excluding device-specific sections.

6. Several of the proposed modifications to the form also appear to exceed current FDA legal requirements for post-marketing reports. Most notable is the possibility that product errors, problems, and switches that do not involved adverse events must be reported for marketed drugs. Based on the new form's layout, it is unclear if this will be required for drugs, devices, or both. Medication errors without adverse events are currently not required by law (although the have been proposed in The Tome). Likewise, there is no codified provision for reporting "problems" and "switches" with drug products. The requirements for such reports should be clarified and consistent with imminent Final Regulations.

Specific comments Section B

1. The new field ***Product Switch*** is open to almost limitless interpretation and needs to be more clearly defined. There is no corresponding E2B field for this parameter. Adding it will require source code modification by our software vendor (Relsys). The same holds true for the ***No Harm*** tick-box.

2. It is not clear if the new field ***Important Medical Events*** is intended to reflect the ICH "Medically Significant" seriousness criterion or some other measure.

3. This section in general will require a significant amount of re-programming and re-formatting.

Specific comments Section C

1. It is unclear how ***Product Available for Evaluation?*** should be used.
    - Are companies expected to solicit returns for all ADEs?
    - Must returned product be kept in storage for possible FDA analysis?
    - When product is returned, are manufacturers expected to submit a follow-up submission to FDA to reflect that information? Submitting MedWatch forms to reflect administrative details (rather than new medical information) is a significant deviation for companies with global workflows.

2. There are currently no E2B fields to allow for capture of this information.

Specific comments Section D

1. Most of the information in this section is currently stored in the safety database. The exception is NDC# or unique ID. It is possible that an existing E2B field could be used to capture this information, but agreement should first be secured at the ICH level. It should also be noted that NDC# is required only in the US. The value of adding this information to supplement that already covered by the drug name and NDA# is dubious.

If you have any questions regarding these comments, please contact Mr. Thomas Umrath at (862) 778-2293.

Sincerely,

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Clinical Safety and Epidemiology